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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,185	06/25/2001	Toshihiko Ashikari	46/221	2199

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EXAMINER
KATCHEVES, KONSTANTINA T

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/19/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,185	ASHIKARI ET AL.	
	Examiner	Art Unit	
	Konstantina Katcheves	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-10 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-10 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-10 are pending in the present application. This Office Action is in response to Paper No. 13, filed 26 February 2003.

Response to Amendment

Claims 1-6 and new claims 9 and 10 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,965,444 in view of Kawahata et al.

Claims 1-8 and new claims 9 and 10 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 8 stands rejected under 35 U.S.C. §102(b) as being anticipated by Omura (EP 0 699 748 A2).

Claims 6 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Ashikari et al (EP 0 814 165 A2) in view of Kawahata et al (Yeast (1999) 15:1-10). The rejection of claims 1~5 under under 35 U.S.C. 103(a) as being unpatentable over Ashikari et al. in view of Kawahata et al. has been withdrawn in view of Applicant's amendment recited the specific sequence of SEQ ID NO:1.

The rejections of claims 3-8 under 35 U.S.C. §112, second paragraph, as being indefinite have been withdrawn in view of Applicant's amendments to the claims.

Response to Arguments

Claims 1-6 and new claims 9 and 10 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,965,444 in view of Kawahata et al.

The '444 patent teaches a method of constructing recombinant yeast cells which do not contain a selective marker gene. The method employs a vector comprising an R gene and an expressible selective marker wherein the R gene and the selective marker are flanked by a pair of R sensitive sequences oriented in the same direction wherein the R sensitive sequence located nearest the R gene lacks 10 or less nucleotides at the end distal from the spacer sequence in the inverted repeat which is at the opposite end from the end adjacent to said R gene and the R sensitive sequence locates nearest the selective marker gene lacks 10 or less nucleotide sequences at the end distal from the spacer sequence in the inverted repeat which is at the opposite end from the end adjacent to said selective marker gene. The vector further comprises sequences at either end of the above construct wherein the sequences are recombinable with the yeast chromosome. The vector may further comprise a foreign gene to be inserted into the yeast chromosome such that after the recombination event between the pair of R sensitive sequences, the R gene and the selective marker are excised from the chromosome while the foreign gene remains. See entire document, especially pp. 4-5.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to use the FRT/Flp recombination system of yeast in the vector and method taught by Askikari et al. One of ordinary skill in the art would have been motivated to do so because

Askikari et al teach the equivalence of the four known site-specific recombination systems (2 element systems in which the recombination sites comprise inverted repeats separated by a spacer sequence which determines orientation). See p. 2, lines 31-37. It is prima facie obvious to use a known equivalent for the same purpose. See MPEP 2144.06. Furthermore, it would be advantageous as the FRT/Flp recombination system is endogenous to Saccharomyces thus one would not need to incorporate the Flp recombinase gene into the vector.

It would also have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a galactose-inducible growth inhibitory sequence into the vector taught by the '444 patent. One of ordinary skill in the art would have been motivated to do so because Kawahata et al teach the advantage of using such a sequence in marker gene recycling is that is serves as a positive selection for the loss of integrated DNA sequences. Selections, rather than screens, are greatly advantageous in saving time and labor in identifying desired recombinants. Furthermore, the '444 patent teaches one advantage of their vector and method is that it permits the same selective marker may be used for multiple insertions (in other words, marker gene recycling). Success would have been expected by one of ordinary skill in the art for the combined teachings of the '444 patent in view of Kawahata et al.

Claims 1-8 and new claims 9 and 10 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement is established by 35 U.S.C. 112, first paragraph which states that the: "*specification* shall contain a written description of the invention. . .[emphasis added]." The written description requirement has been well established and characterized in the case law. A specification must convey to one of skill in the art that "as of the filing date sought, [the inventor] was in possession of the invention." See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in "possession" of the invention claimed by describing the invention with all of its claimed limitations "by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

New claims 9 and 10 are also subject to the present rejection although they do not recite the "substantially identical to" language and are drawn to un specified mutants and deletions because, as discussed in the prior Office action, this disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all sequences based on the teachings in the specification. There is no discussion of what specific sequences within SEQ ID No. 1 are essential to Flp recognition and recombination induction other than the deletions of the 5' and 3' ends. Therefore, the specification does not describe the claimed substantially identical sequences in such full, clear, concise and exact terms so as to indicate that Applicant has possession of these sequences.

Applicant argues, "those of skill in the art could indeed have carried out the DNA construct having a sequence 'substantially identical to' the native FRT sequence." As set forth above, the standard for written description is not whether those skilled in the art could construct

sequences substantially identical to Applicant's, but rather, whether those of skill in the art would reasonably conclude that Applicant had possession of the claimed invention.

Applicant points to example 1 to show that those of skill in the art can construct a substantially identical construct, which teaches that a recombination event actually occurred when yeast was transformed by DNA constructs having deletions. Applicant should note that the example also shows that recombination frequency "sharply decreases as deletion increases." Thus, Applicant's disclosure must show more than DNA constructs having deletions in the FRT sequence can facilitate recombination in order to show possession of the invention claimed. Additionally, the reference, Storici et al., cited by Applicant, is provided as a publication to show the state of the art at the time the invention was made. Indeed, Storici et al. do teach three examples where substitution mutations within the spacer regions of FRT resulted in recombination events. However, neither Storici et al. nor the disclosure teach which regions can tolerate such mutations and which regions are required for activity. Applicant has merely provided the reference and disclosure of the specification as evidence that one of skill in the art can make a construct that has a sequence 'substantially identical to' a native FRT sequence. Applicant's line of reasoning in traverse of the present rejection appears to be more suited to an enablement rejection, which this is not.

Claim 8 stands rejected under 35 U.S.C. §102(b) as being anticipated by Omura (EP 0 699 748 A2).

Applicant argues that the invention is to a beer made by the method of transforming a yeast lacking a selectable marker gene. Applicant has not shown how a beer made using this

method would be novel or distinct from a beer made using any other method. Applicant is reminded that the instant claim is a product by process claim. The process by which a product is made must confer a patentable distinction to the product in order for the product to be considered patentable. In spite of the fact that the instant claims recite process limitations, it is the patentability of the product claimed and not of the recited process steps, which must be established. Since the prior art discloses a product, which reasonably appears to be either identical with or only slightly different from the product claimed by Applicant in the instant claims, rejection is appropriate. Absent any demonstration to that the beer of Omurais novel or distinct, the beer produced with the instant methods would be the same as the beer produced using any other method known in the art. As such, the claims read on any beer using recombinant yeast of the genus Sacharomyces. Thus, Applicant's claims directly read on the beer disclosed in Omura regardless of any difference in the method of producing the product.

Claims 6 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Ashikari et al (EP 0 814 165 A2) in view of Kawahata et al (Yeast (1999) 15:1-10).

Claim 6 is also a product-by-process claim. As such, patentability does not rely on the method steps unless the method steps lead to a difference in the product. See MPEP 2113. For the same reasoning discussed above with regard to claim 8, Applicant has failed to show how a yeast transformed with the specific FRT sequence of SEQ ID NO:1 would be novel or distinct from a yeast transformed with the FRT sequence of Ashikari et al. Thus, claim 6 stands rejected under 35 U.S.C. 103(a).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Konstantina Katcheves whose telephone number is (703) 305-1999. The examiner can normally be reached on Monday through Friday 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3388.

Konstantina Katcheves
May 16, 2003

JAMES KETTER
PRIMARY EXAMINER